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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,249	01/26/2004	Naoto Tonouchi	247264US0CONT	8012

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/763,249	TONOUCHI ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *35-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/0805 and 01/26/*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: sequence alignments and a copy of document in 892.

Response to Restriction Requirement filed on Feb. 12, 2006 is acknowledged. Claims 1-45 are pending; the elected claims 1-34 are under examination. Claims 35-45 are withdrawn from examiner's consideration as directed to a non-elected invention; see 37 CFR 1.142 (b).

DETAILED ACTION

1. Restriction/Election

Applicant's election, with traverse, of Group I, claims 1-34 in the reply filed on Feb. 16, 2006 is acknowledged. The traversal is on the ground(s) that the Office has characterized the inventions of Group I-III as unrelated, but failed to provide any reasons and/or examples to support this assertion. Accordingly, the Office has failed to meet the burden necessary in order to sustain the restriction requirement.

This is not found persuasive because Group I is directed, as explained in the Restriction Requirement of Dec. 16, 2005, to four products, polypeptides of SEQ ID NO: 15 and 17, and their encoding DNA, furthermore to expression vectors, transformed cells and method of use transformed cells for production of polypeptides of SEQ ID NO: 15 and 17 and the use of said polypeptides for production of dipeptides. The scope of invention is very broad and, actually, comprises claims that should be, accordingly to US restriction practice, restricted to 4 inventions. However, because both of the peptides and their encoding DNA molecules are originating from Pseudomonas putida, per examiner's discretion they are included in one invention.

Group II comprises claims 35-46, directed to the use of a protein having proline iminopeptidase that is not that of SEQ ID NO: 15 and 17, thus, claims 35-44 are directed to the use of the product that is different than any of products of Group I.

Group III, claims 47-49, is directed to the use of naturally occurring bacteria of Corynebacterium, Pseudomonas and Bacillus for production of dipetides. Thus, group III does not involve use of any of enzymes or DNA molecules of Group I. Actually, the disclosure does even not provide any amino acid or nucleotide sequence of a dipeptide forming enzyme from Bacillus.

In conclusion, the invention of Group III is different than any of invention of Group I and II. The inventions as claimed and described in the specification cannot be practice together. There is no need to provide any examples to illustrate the point, because Applicants disclose the invention in that very way.

The requirement is still deemed proper and is therefore made FINAL.

2. Priority

Acknowledgment is made of Applicant's claim for priority based on Japanese applications 2001-226568 filed 07/26/2001 and 2001-310547 filed 10/05/2001. However priority documents are not translated and do not contain any sequence listing. Thus the priority of the instant claims to the Japanese applications have not been granted.

The instant application is a continuation of the PCT/JP01/07635, filed 07/26/2002. This application has been published on Feb. 06, 2003 as document

WO03/10307. However, the document is published in Japanese and Applicants have not provided a translation. For that reason priority of the instant claims to the PCT application is not granted. In results, the instant claims have priority to the filing date of this utility application, which is 01/26/2004.

3. Objections

The specification is objected to for lack of reference to prior applications. A reference to the prior applications must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

Claims 4 and 5 are objected to for using the term "base sequence" to mean "nucleotide sequence". Please correct both claims.

Claims 11-14 are objected to for the phrase «in a state where the DNA is able to express«. No DNA molecule is able to express anything. It is the transformed cell that expresses the protein encoded by the DNA with which it has been transformed.

3. Rejections

3.1. 35 USC, section 101

35 U.S.C. §101 states:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 3 and 4 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter. The claims, as written, do not sufficiently distinguish over protein and nucleic acids, as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated"; see MPEP 2105.

4.2. 35 USC, section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-2, 3-4, 11-14, 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In addition, claims 1-2 are rejected as unclear. The disclosure fails to define the meaning of the term "inversion of one or a plurality of amino acids". The term inversion as related to SEQ ID NOs: 15 and 16 having 337 amino acids comprises enormous number of changes involving these 337 amino acids. Without a limitation as to the nature of inversion the claim remains indefinite.

Claims 11-14 are unclear as to whether the transformed cell is in a transformed organism or it is a transformed, isolated cell in vitro. Claims 15-34 are objected to as dependent on unclear claims 11-14.

Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph because the phrase "hybridizes with the complementary strand " renders the claim indefinite. There are many sets of hybridization conditions in the prior art that are used for identifying DNA molecules by hybridization. Applicants exemplify hybridization conditions on page 21, but there is nothing to suggest that other conditions are excluded from the scope of the claim. Including the hybridization conditions in the claims would overcome this rejection. Claims 7-8, 11,12, 15, 16, 19, 20, 23, 24, 27, 28, 31, 32 are included this rejection as not correcting the language of the claim from which they depend.

Claims 19-22 are rejected as confusing. A method for producing a dipeptide cannot be described by "producing a dipeptide". Secondly, due to the confusing language of the claim it is unknown whether

a) the protein having activity to form dipeptide is produced by the transformed cell, or

b) L-amino acid and/or L-amino acid ester are produced in the transformed cell, and

c) it is unclear were the dipeptide is produced; in the transformed cell or somewhere else?

Claims 23-34 are included in his rejection as depending on the rejected base claims.

4.3. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4.3.1. Lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 part D and 2 part F are rejected because they are generic and directed to large genera of proteins having the activity of producing a dipeptide from an L-amino acid ester and L-amino acid, wherein the structure of the proteins is not sufficiently described. The specification discloses only two representatives of the claimed genera, i.e., SEQ ID NO: 15 and SEQ ID NO: 17. These two sequences do not provide an identifying structural characteristics of the two genera of proteins obtained by any substitution, deletion, insertion addition or inversion of one or plurality of amino acids. Furthermore, the disclosure fails to provide the relationship between function and structure of SEQ ID NO: 15 and 17, and for that reason any teaching of amino acid changes neutral for the enzymatic activities of the proteins. One skilled in the art is aware that a change of even one amino acid in a protein sequence may turn the protein inactive or change its enzymatic activity. Thus, teachings as to which changes in SEQ ID NO: 15 and 17 are neutral from the point of view of their enzymatic activities are

necessary for structural description of the claimed genera. The disclosure, however, fails to describe the modifications, which are neutral. In conclusion, the predictability of the structure of the species of the claimed genera is not apparent and one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

4.3.2. Scope of enablement

Claims 1 part D and claim 2 part F are rejected because the specification, while being enabling for SEQ ID NO: 15 and 17 identifying two peptide forming enzymes originating from Pseudomonas putida, does not reasonably provide enablement for a any peptide forming enzyme obtained by modifications of SEQ ID NO: 15 and 17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or

absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breadth of the claims covers any variant of the SEQ ID NO: 15 and 17 having the desired activity of forming dipeptides. Although manipulations with enzyme structures are advanced, and skills of artisans high, because of lack of disclosure of function/structure of SEQ ID NO: 15 and 17 Applicants force one skilled in the art to experimentation, which is not routine. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed proteins species have dipeptide forming ability. The provision of SEQ ID NO: 15 and 17 fails to provide such guidance of polypeptides with major structural variations therefrom which remain encompassed within the scope of the rejected claims. Without a further guidance on the part of Applicants with regards to the structure of the claimed inventions experimentation left to those having skills in the art has a low probability of success, therefore, it is improperly extensive and undue.

3.3. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1D is rejected under **35 U.S.C. 102(b)** as being anticipated by Pseudomonas putida prolyl aminopeptidase having accession number Q88D01 and disclosed in Nelson K.E. et al., "Complete genome sequence and comparative analysis of the metabolically versatile Pseudomonas putida KT2440", Environ. Microbiol. 2002, 4, 799-808. The protein is 95% identical to that of SEQ ID NO: 15 of the instant application and has the same activity; see the printout of the sequence alignment.

In addition, claims 1D and 2 F are rejected under 35 U.S.C. 102(b) as being anticipated by prolyl aminopeptidase from Pseudomonas aeruginosa, having accession number B83010, and disclosed in Stover R. et al., "Complete genome sequence of Pseudomonas aeruginosa PA01, an opportunistic pathogen, Nature, 2000, 406, 959-964. The protein is 81.2% identical to that of SEQ ID NO: 17 of the instant application and has the same activity; see the printout of the sequence alignment.

4. Conclusion

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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